REMARKS

Claims 110 - 151 are pending.

Claims 126 - 151 are withdrawn.

Claims 110 - 125 are under active consideration.

Claims 115 and 119 are canceled with entry of this amendment.

New claims 152 - 156 are added with entry of this amendment.

Claim Objections

Claims 112, 116, 124 and 125 are objected to due to because of the misspelled words "xtraction" (the correct spelling is "extraction") and "quinaline" (the correct spelling is "quinalone") and the use of an undefined acronym (IGF-1). These errors are corrected by the present amendment.

Rejections under 35 USC 112, first paragraph

Claims 110 - 125 have been rejected under 35 USC 112, first paragraph. The examiner argues that while being enabling for exposing steps of harvesting the pancreas and extracting the islet beta cells, the application does not reasonably provide enablement for exposing islets to nicotinamide *before* harvesting and extracting. Specifically, the examiner points to the Wands factors concerning undue experimentation.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosure coupled with information known in the art without undue experimentation. *United Stated v. Telectronics, Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988); *In re Stephens*, 188 USPQ 659 (CCPA 1976). The test of enablement is not whether any

experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt,* 190 USPQ 214 (CCPA 1976). An extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance. *In re Colianni*, 195 USPQ 150 (CCPA 1977) (Miller, J., concurring). The experimentation required, in addition to not being undue, must not require ingenuity beyond that expected of one of ordinary skill in the art. *In re Angstadt*, supra. For example, in one instance a "few hours" of experimentation to determine process parameters was not considered to be undue in view of the nature of the invention (preparation of oxygenated hydrocarbons). *In re Borkowski*, 164 USPQ 642 (CCPA 1970). In *Tabuchi v. Nubel*, 194 USPQ 521 (CCPA 1977) a screening procedure which took 15 calendar days was not considered undue experimentation because the test was both simple and straightforward and because of its demonstrated success in producing the desired result.

Independent claim 110 has been amended to remove the alternative clauses so that it now recites a method comprising harvesting the pancreas, followed by exposing the pancreatic islet cells to nicotinamide, followed by extracting pancreatic islet cells from the harvested pancreas.

The applicant respectfully rebuts the present rejection and asserts that 110 - 125 are fully described and enabled. The specification at page 2, lines 28 - 29 that teaches a method comprising harvesting the pancreas and extracting the islet cells "wherein the islets (*at least at some stage* in the performance of the method) are exposed to nicotinamide." This clearly would encompass exposure of the beta cells to nicotinamide *at any time* during or between the harvesting and extracting stages.

The method of exposing cells or harvested organs to a chemical agent such as nicotinamide is enabled because at the time of filing methods were well known and routinely used by which explanted organs or cells could be exposed *in vitro* to any number of desired

chemicals by simply adding such a chemical to the fluid in which the cells are bathed. Such methods were so well known and routine at the time of filing that a detailed explanation would not have been necessary, and it would be enough to say that the organ or cells were exposed to a particular agent. At the time of filing, anyone of skill in the art would certainly have been familiar with such basic techniques. In the specification at page 12, lines 8 – 11, the washing and culture of tissue is briefly described using 2% human serum albumin and 10 mM nicotinamide. It would not be considered necessary to describe how such a solution was made or how the tissue was washed or bathed in the culture medium. The examiner is respectfully reminded that bathing the pancreas in a medium containing nicotinamide would be sufficient to expose the pancreatic islet cells to nicotinamide as claimed, because the pancreas is a non-encapsulated endocrine organ and as such, the inherent structure of the organ allows fluids and solutes to flow into and out of the organ thereby exposing the beta cells of the organ to the fluids or solutes in which the organ is bathed. Additional references that discuss methods of exposing pancreatic tissue to chemical agents contained in a solution include US Patent No. 6,090,400 to Elliott at column 4, lines 40-50; and Clark et al., *Islet Culture in Defined Serum-Free Medium,* Endochrinology (1990) 126 (4) 1895-1903.

In view of these facts, it is believed that one of skill in the art would not have to conduct "undue experimentation" in order to practice a method comprising harvesting the pancreas, followed by exposing the pancreatic islet cells to nicotinamide, followed by extracting pancreatic islet cells from the harvested pancreas. It is respectfully requested that the rejections of claims 110 – 125 under 35 USC 112, first paragraph be withdrawn.

Claim 118 has been rejected under 35 USC 112, first paragraph because "the specification fails to provide any teaching or support for such a claim." The examiner goes on to

say that the specification teaches "no increased benefit was found on culturing islets with IGF-1 beyond a 24 hrs period post isolation" and that in the examiner's opinion, the specification "appears to teach away from the instant claim." This rejection is based on a misinterpretation of the specification and/or the claim. The specification does not suggest that a reduced benefit is produced by increasing exposure to IGF-1 for those cells from piglets furthest from full term, it merely teaches that *no increased benefit* was found on culturing islets with IGF *beyond a 24 hr period* post isolation. Additionally, the specification cannot teach away from the claim, because the claim does not recite an increased benefit gained by increasing exposure to nicotinamide for those cells from piglets furthest from full term. Additionally, the applicants do not see how such facts, even if true, would undermine the claim in terms of written description or enablement. It is therefore respectfully requested that the rejections of claim 118 under 35 USC 112, first paragraph be withdrawn.

In view of the above facts and argument, it is respectfully requested that the rejections of claims 110 – 125 under 35 USC 112, first paragraph be withdrawn.

New Claims 152 and 153

New claim 152 recites a method in which islet cells are exposed to nicotinamide *simultaneously* with the *extraction* procedure. This claim is supported in originally-filed claim 2 and in the specification at page 6, line 11, which describes treating islet cells with nicotinamide simultaneously with the step of extracting. Although this new claim is not subject to the present rejection under 112, the applicants would like to point out that this claim is fully supported in terms of written description and is enabled as for claim 110, above.

New claim 153 recites a method in which the pancreas of a piglet is exposed to nicotinamide *simultaneously* with being *harvested.* This claim is supported in the specification at page 2, lines 28 – 29, is fully supported in terms of written description and is enabled as for claim 110, above.

Rejections under 35 USC 112, second paragraph

Claims 110 – 125 have been ejected under 35 USC 112, second paragraph as vague or indefinite. The claims have been amended to address these problems.

Claim 110 as been amended to recite the required clause that relates back to the preamble: "...; the method resulting in a xenotransplantable islet cell."

Claim 113 was deemed vague because of the phrase "the harvested pancreas is in a supportive mammalian albumin." Claim 113 has been amended so that it now recites "The method of claim 110 wherein the harvested pancreas is bathed in a mammalian albumin substantially free of microbiological agents." This phrase should remove the vagueness. The term "mammalian albumin" is defined in the definitions section on page 23 of the specification.

Claim 113 was deemed vague because of the phrase "non-human microbiological agents." This phrase has been amended simply to "microbiological agents," thereby removing the vagueness.

Claim 118 was deemed vague due to the use or the word "greater." The claim has been amended to recite "The method as claimed in claim 116 wherein the amount of compound used to treat the islets is greater when using a piglet further from full-term gestation, and is less when using a piglet closer to full-term gestation." The applicant believes that this should remove the vagueness.

Claim 119 was deemed vague due to lack of antecedent basis for the word "their." This claim is cancelled.

Claim 124 was deemed vague due to the use or the word "associating." This word has been changed to "contacting" thereby removing the vagueness.

Claim 125 was deemed vague due to the use or the word "quinaline." This was a typographical error and the correct word "quinalone" has been substituted for "quinaline."

It is believed that the above amendments are sufficient to remove the rejections under 35 USC 112, second paragraph, and it is requested that these rejections be withdrawn.

Rejections under 35 USC 102(b)

Claims 110, 111, 113, 115 and 120 have been rejected under 102(b) as anticipated by Rayat et al. (1998). The examiner states that Rayat et al teach a method of preparing porcine islet cells as a potential source of transplantable cells for humans, the method comprising harvesting the pancreas of a 1-3 day old piglet, extracting the beta cells and culturing the islet cells with a medium that includes bovine serum albumin (a trauma-protecting agent) and nicotinamide.

Claim 119 is cancelled.

Claim 110 has been amended to recite a method whereby the pancreatic beta cells are exposed to nicotinamide after harvesting the pancreas but before extracting the beta cells. Rayat et al. teaches exposing the islet cells to nicotinamide only *after* the extraction step. Rayat et al. does *not teach* exposing the islet cells to nicotinamide *before* the extraction step. For an anticipation rejection, each and every element of the claim must appear in the cited reference. Rayat et al does not contain this limitation, therefore Rayat et al. does not anticipate claim 110 as

amended. Because claims 111, 113, 115 and 120 depend from claim 110, these claims equally cannot be anticipated by Rayat et al. It is respectfully requested that the present rejection under 35 USC 102(b) be withdrawn.

Rejections under 35 USC 102(e)

Claims 110, 111, 113, 115 and 120 have been rejected under 102(e) as anticipated by Elliott (US Patent Nos. 6,146,653 and 6,090,400). As the examiner notes, the references have a common inventor with the instant application. Indeed, the sole inventor on both of the referenced patents is Robert Bartlet Elliott of Auckland, New Zealand, who is one of the inventors of the present application. This rejection under 102(e) may therefore be overcome by filing a declaration under 37 CFR 1.132 showing that the cited references are not "by another." The applicant will gladly supply such a declaration in the near future, but unfortunately cannot do so with the instant response due to temporary unavailability of the inventor. This declaration should overcome the rejection under 35 USC 102(e).

Rejections under 35 USC 102(f)

Claims 110, 111, 113, 115 and 120 have been rejected under 102(f). The examiner asserts that US Patent Nos. 6,146,653 and 6,090,400 disclose the subject matter as now claimed, and clarification is requested regarding inventorship. The inventor on both of the referenced patents is the same as one of the inventors of the present application: Robert Bartlet Elliott. The applicant will attest to this in a declaration under 37 CFR 1.132. Such a declaration should overcome the rejection under 35 USC 102(f).

Rejections under 35 USC 103(a)

Claims 110 and 112 have been rejected as obvious over Rayat et al in view of Brandhorst et al. Claims 110, 113, 114, 116, 118 and 123 been rejected as obvious over Rayat et al in view of Clark et al. and Maysinger et al. Rayat et al describes a method of preparing porcine islet cells comprising harvesting the pancreas of a 1-3 day old piglet, extracting the islet cells and culturing them with a medium that includes bovine serum albumin (BSA) and nicotinamide. Brandhorst suggests using Liberase to digest porcine pancreas. Clark et al teaches using a medium containing GFF-1 and serum albumin. Maysinger et al. teaches culturing islet cells in a medium containing IGF-1 and growth factors.

Claim 110 has been amended to recite a method whereby the pancreatic beta cells are exposed to nicotinamide *before* extracting the beta cells. Rayat et al. teaches exposing the islet cells to nicotinamide only *after* the extraction step. Rayat et al does not teach or suggest exposing beta cells to nicotinamide before the extraction step. Neither do any of the cited references, alone or in combination, teach or suggest exposing beta cells to nicotinamide before the extraction step. For an invention to be obvious, every element of the claimed invention must be found in the combined references (In re Vaeck, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991)), and this is not the case here. It would not, therefore, have been obvious, in view of the cited references, to practice the invention as presently claimed. It is respectfully requested that the present rejections under 35 USC 103(a) be withdrawn.

Claim 112 has been rejected as obvious over Rayat et al in view of Brandhorst et al., which suggests the use of Liberase. Applicant asserts that unexpected and beneficial results described in the present application supply secondary indications of non-obviousness for this claim. Specifically at section 3c (page 11 line 25 to page 12 line 6) of the specification, it is

taught that much greater yields of islet cells can be obtained using the present methods with Liberase than would be expected in view of the Brandhorst et al. disclosure. The specification teaches that using Liberase with the methods of Brandhorst et al., the yield of islet cells per neonatal pig pancreas can expect to be doubled (400 islets to 800 per) in comparison to simply using collagenase. But when employing the methods described and claimed by the present application, this yield increases by 75-fold (400 islets to 30,000). The specification describes these results as "extraordinary larger [yields]" and states that such yields are "very much greater than that to be expected from following the procedure of Brandhorst et al. with pigs." In view of these unexpected and beneficial results, as well as the arguments and amendments discussed above, applicants request that the present rejection of claim 112 be withdrawn.

Claim 117 was rejected under over Rayat et al in view of Clark et al., Maysinger et al. and further in view of Saura et al. Claim 117 is drawn to treating islet cells with GPE. Saura et al. teaches that GPE has the activity of IGF-1 in brain tissue. The examiner argues that given this knowledge, it would have been obvious to modify the methods of Rayat et al in view of Clark et al., and Maysinger et al and substitute GEP for IGF-1. Applicant rebuts this assertion because the knowledge that GPE has similar activity to IFG-1 *in the brain* would not obviously lead one of skill in the art of extracting, maintaining and transplanting pancreatic islet cells to use GPE in the islet maintenance medium. Applicants therefore believe that claim 117 is not obvious in view of the cited art and respectfully request that the present rejection of claim 112 be withdrawn.

Claims 121 and 122 were rejected under over Rayat et al in view of Pu et al. Claims 121 and 122 are drawn to treating islet cells with lignocaine as a trauma-preventing agent. Pu et al teach that lignocaine may be used to restore contractility to heart tissue after trauma, and suggest

it could be used therapeutically to treat blunt chest trauma. The examiner asserts that with this knowledge, it would have been obvious to use lignocaine as a trauma-preventing agent when extracting islet cells from the pancreas. It is the applicants contention, however, that the knowledge that lignocaine can act to restore heart contractions would in no way suggest to one of skill in the art that this compound would be of any use in maintaining and transplanting pancreatic islet cells. Applicants therefore believe that claims 121 and 122 are not obvious in view of the cited art and respectfully request that the present rejections be withdrawn.

Claims 124 and 125 were rejected under over Rayat et al in view of Champion et al. Claims 124 and 125 are drawn to culturing islet cells with antibiotics. In view of the arguments presented above for claim 110, it is believed that neither claim 110 nor dependent claims including 124 and 125 are obvious in view of the cited references, and it is respectfully requested that the present rejections be withdrawn.

Non-Statutory Obviousness-Type Double Patenting Rejection

Claims 110, 111, 115, 120 and 123 have been deemed by the examiner to be non-identical to but not patentably distinct from the claims of US Patent No. 6,146, 653, the inventor of which is identical to one of the inventors of the instant application (Elliott). A Terminal Disclaimer may be used to overcome such a non-statutory double patenting rejection. In the present case, however, applicant believes that the rejection is traversed in view of the present amendments. The claims as presently amended are significantly distinct from those of Patent No. 6,146, 653, and any such claims that would issue would not be co-extensive in scope with those of the previously issued patent. In view of this, the present non-statutory double patenting

rejection would not be rightly applicable, and it is respectfully requested that the rejection be withdrawn.

CONCLUSION

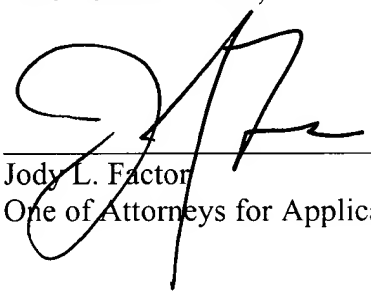
In light of the above amendments and remarks, applicants submit that the present application is in a condition for allowance, and request that the examiner withdraw the outstanding rejections.

If the examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, applicants invite the Examiner to contact applicants' attorney.

Should anything further be required, a telephone call to the undersigned, at (312) 226-1818, is respectfully invited.

Respectfully submitted,

FACTOR & LAKE, LTD.



Dated: January 29, 2004

Jody L. Factor
One of Attorneys for Applicant

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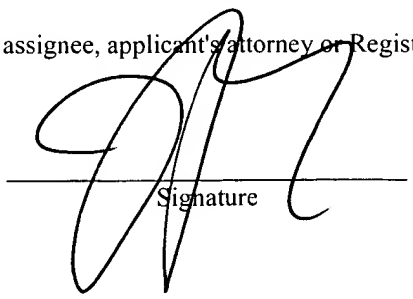

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